

## THE INVENTION CLAIMED IS

1. A research model for screening compounds suspected of modulating the CD40L/CD40R signaling pathway by interfering with the CD40L/CD40R signaling pathway in an animal, human, or system, comprising the following steps:

contacting a first sample of cells with CD40 ligand and measuring the level or amount of a marker;

contacting a second sample of cells with a compound and CD40 ligand and measuring the level or amount of a marker; and

comparing the level or amount of the marker of the first sample of cells with the level or amount of the marker of the second sample of cells.

2. The method of claim 1, wherein the sample of cells are central nervous system cells, cell lines derived from central nervous system cells, peripheral cells, cell lines derived from peripheral cells, transgenic cells, transgenic cells derived from transgenic animals, human cells or cell lines, or immortalized or non-immortalized cell lines derived from humans, higher primates, primates or murine sources.

3. The method of claim 1, wherein the marker is the levels or amounts of one or more cytokines.

4. The method of claim 3, wherein the cytokine is selected from the group consisting of tumor necrosis factor, interleukin 1, interleukin 6, interleukin 12, interleukin 18, macrophage inflammatory protein, macrophage chemoattractant protein, granulocyte-macrophage colony stimulating factor, macrophage colony stimulating factor, and combinations thereof.

5. The method of claim 1, wherein the marker is selected from the group consisting of levels, amounts or activities of glutamate release, nitric oxide production, nitric oxide synthase, superoxide, superoxide dismutase, glutamate release, nitric oxide production, nitric oxide synthase, superoxide, superoxide dismutase, and combinations thereof.

6. The method of claim 1, wherein the marker is selected from the group consisting of a major histocompatibility complex molecule, CD45, CD11b, F4/80 antigen, integrins, a cell surface molecule, and combinations thereof.

7. The method of claim 1, wherein the marker is decreased neuronal inflammation, the levels or amounts of A $\beta$ ,  $\beta$ -amyloid precursor protein ( $\beta$ -APP), a fragment of  $\beta$ -APP, a fragment of A $\beta$ , or combinations thereof.

8. The method of claim 1, wherein the compound is a compound that binds to CD40R, a compound that binds to CD40L, a compound that decreases trimerization of CD40R, a compound that decreases trimerization of CD40L, a compound that modulates the CD40L/CD40R signaling pathway upstream or downstream of CD40L/CD40R interaction, a compound that reduces the phosphorylation of the tau protein or mutants thereof, a compound that interferes with TNF receptor-associated factors, a compound that interferes with presenilin-1 and/or presenilin-2, a compound that inhibits  $\beta$ -secretase activity, a compound that inhibits  $\gamma$ -secretase activity, a compound that enhances  $\alpha$ -secretase activity, a compound that alters APP processing, a compound that reduces the ratio of APP  $\beta$ -CTF to APP  $\alpha$ -CTF, a compound that reduces the amount of  $\beta$ -CTF, a compound that promotes brain-to-blood clearance of  $\beta$ -amyloid, a compound that increases circulating levels of  $\beta$ -amyloid, a compound that reduces the size and/or number of amyloid plaques, a compound that reduces  $\beta$ -amyloid burden, a compound that reduces soluble  $\beta$ -amyloid levels, a compound that reduces total  $\beta$ -amyloid levels, a compound that reduces congophilic  $\beta$ -amyloid deposits, a compound that reduces reactive gliosis, microgliosis, astrogliosis and combinations thereof, a soluble CD40R compound, a soluble CD40L compound, an immunogenic CD40L compound, a soluble CD40L variant (CD40LV) compound, an interfering RNA (dsRNA, RNAi or siRNA) compound to CD40R, an antisense RNA compound to CD40R, an interfering RNA (dsRNA, RNAi or siRNA) compound to CD40L, an antisense RNA compound to CD40L or combinations of interfering RNA (dsRNA, RNAi or siRNA) compounds and antisense compounds, or a compound selected from the group consisting of agonistic antibodies to CD40R, agonistic antibodies to CD40L, antagonistic antibodies to CD40R and antagonistic antibodies to CD40L.

9. The method of claim 8, wherein the interfering RNA (dsRNA, RNAi or siRNA) comprises polynucleotide sequences identical or homologous to CD40L, CD40R or  $\beta$ -amyloid.
10. The method of claim 9, wherein the interfering RNA (dsRNA, RNAi or siRNA) has greater than 70% homology to CD40L, CD40R or  $\beta$ -amyloid.
11. The method of claim 9, wherein the interfering RNA (dsRNA, RNAi or siRNA) has greater than 95% homology to CD40L, CD40R or  $\beta$ -amyloid.
12. The method of claim 8, wherein gene fragments of CD40L, CD40R or  $\beta$ -amyloid are targeted with the interfering RNA (dsRNA, RNAi or siRNA), and wherein the gene fragments are approximately 15-25 nucleotides in length.
13. The method of claim 8, wherein gene fragments of CD40L, CD40R or  $\beta$ -amyloid are targeted with the interfering RNA (dsRNA, RNAi or siRNA), and wherein the gene fragments are greater than 25 nucleotides in length.
14. The method of claim 8, wherein gene fragments of CD40L, CD40R or  $\beta$ -amyloid are targeted with the interfering RNA (dsRNA, RNAi or siRNA), and wherein the gene fragments are greater than 50 nucleotides in length.
15. The method of claim 8, wherein gene fragments of CD40L, CD40R or  $\beta$ -amyloid are targeted with the interfering RNA (dsRNA, RNAi or siRNA), and wherein the gene fragments are one nucleotide less than the full length gene of CD40L, CD40R or  $\beta$ -amyloid.
16. The method of claim 1, wherein the animal or human is afflicted with a disease or disorder selected from the group consisting of neuronal inflammation, brain injury, brain trauma, tauopathy, and an amyloidogenic disease.
17. The method of claim 16, wherein the amyloidogenic disease is selected from the group consisting of Alzheimer's disease, scrapie, transmissible spongiform encephalopathy, hereditary cerebral hemorrhage with amyloidosis Icelandic-type, hereditary cerebral

hemorrhage with amyloidosis Dutch-type, familial Mediterranean fever, familial amyloid nephropathy with urticaria and deafness (Muckle-Wells syndrome), myeloma or macroglobulinemia-associated idiopathy associated with amyloid, familial amyloid polyneuropathy (Portuguese), familial amyloid cardiomyopathy (Danish), systemic senile amyloidosis, familial amyloid polyneuropathy (Iowa), familial amyloidosis (Finnish), Gerstmann-Strausner-Scheinker syndrome, medullary carcinoma of thyroid, isolated atrial amyloid, Islets of Langerhans, diabetes Type II, and insulinoma.

18. The method of claim 16, wherein the tauopathy is selected from the group consisting of Alzheimer's disease, frontotemporal dementia, frontotemporal dementia with Parkinsonism, frontotemporal lobe dementia, pallidopontonigral degeneration, progressive supranuclear palsy, multiple system tauopathy, multiple system tauopathy with presenile dementia, Wilhelmsen-Lynch disease, disinhibition-dementia-parkinsonism-amyotrophy complex, Pick's disease, and Pick's disease-like dementia.

19. The method of claim 1, wherein the animal is a non-transgenic animal or a transgenic animal selected from the group consisting of worms, flies or mice.

20. The method of claim 19, wherein the transgenic animal expresses transgenic APP, overexpresses transgenic presenilin protein, overexpresses CD40R, overexpresses transgenic CD40L, and/or expresses tau protein or mutants thereof.

21. A research model for screening compounds suspected of modulating the CD40L/CD40R signaling pathway by interfering with the CD40L/CD40R signaling pathway in an animal, human, or system, comprising the following steps:

- contacting CNS cells expressing CD40R with CD40L and a compound and measuring a marker;

- contacting peripheral cells expressing CD40R with CD40L and the compound and measuring a marker;

- contacting CNS cells with a stimulator of the CD40L/CD40R signaling pathway and the compound and measuring a marker;

- contacting peripheral cells with a stimulator of the CD40L/CD40R signaling pathway and the compound and measuring a marker;

- contacting CNS cells with an inhibitor of the CD40L/CD40R signaling pathway

and the compound and measuring a marker;

contacting peripheral cells with an inhibitor of the CD40L/CD40R signaling pathway and the compound and measuring a marker;

comparing the markers to identify those compounds that modulate the CD40L/CD40R signaling pathway.

22. The method of claim 21, wherein the marker is the levels or amounts of one or more cytokines.

23. The method of claim 22, wherein the cytokine is selected from the group consisting of tumor necrosis factor, interleukin 1, interleukin 6, interleukin 12, interleukin 18, macrophage inflammatory protein, macrophage chemoattractant protein, granulocyte-macrophage colony stimulating factor, macrophage colony stimulating factor, and combinations thereof.

24. The method of claim 21, wherein the marker is selected from the group consisting of levels, amounts or activities of glutamate release, nitric oxide production, nitric oxide synthase, superoxide, superoxide dismutase, glutamate release, nitric oxide production, nitric oxide synthase, superoxide, superoxide dismutase, and combinations thereof.

25. The method of claim 21, wherein the marker is selected from the group consisting of a major histocompatibility complex molecule, CD45, CD11b, F4/80 antigen, integrins, a cell surface molecule, and combinations thereof.

26. The method of claim 21, wherein the marker is decreased neuronal inflammation, the levels or amounts of A $\beta$ ,  $\beta$ -amyloid precursor protein ( $\beta$ -APP), a fragment of  $\beta$ -APP, a fragment of A $\beta$ , or combinations thereof.

27. The method of claim 21, wherein the compound is a compound that binds to CD40R, a compound that binds to CD40L, a compound that decreases trimerization of CD40R, a compound that decreases trimerization of CD40L, a compound that modulates the CD40L/CD40R signaling pathway upstream or downstream of CD40L/CD40R interaction, a compound that reduces the phosphorylation of the tau protein or mutants thereof, a compound that interferes with TNF receptor-associated factors, a compound that interferes with

presenilin-1 and/or presenilin-2, a compound that inhibits  $\beta$ -secretase activity, a compound that inhibits  $\gamma$ -secretase activity, a compound that enhances  $\alpha$ -secretase activity, a compound that alters APP processing, a compound that reduces the ratio of APP  $\beta$ -CTF to APP  $\alpha$ -CTF, a compound that reduces the amount of  $\beta$ -CTF, a compound that promotes brain-to-blood clearance of  $\beta$ -amyloid, a compound that increases circulating levels of  $\beta$ -amyloid, a compound that reduces the size and/or number of amyloid plaques, a compound that reduces  $\beta$ -amyloid burden, a compound that reduces soluble  $\beta$ -amyloid levels, a compound that reduces total  $\beta$ -amyloid levels, a compound that reduces congophilic  $\beta$ -amyloid deposits, a compound that reduces reactive gliosis, microgliosis, astrogliosis, and combinations thereof, a soluble CD40R compound, a soluble CD40L compound, an immunogenic CD40L compound, a soluble CD40LV compound, an interfering RNA (dsRNA, RNAi or siRNA) compound to CD40R, an antisense RNA compound to CD40R, an interfering RNA (dsRNA, RNAi or siRNA) compound to CD40L, an antisense RNA compound to CD40L or combinations of interfering RNA (dsRNA, RNAi or siRNA) compounds and antisense compounds, or a compound selected from the group consisting of agonistic antibodies to CD40R, agonistic antibodies to CD40L, antagonistic antibodies to CD40R and antagonistic antibodies to CD40L.

28. The method of claim 27, wherein the interfering RNA (dsRNA, RNAi or siRNA) comprises polynucleotide sequences identical or homologous to CD40L, CD40R or  $\beta$ -amyloid.

29. The method of claim 28, wherein the interfering RNA (dsRNA, RNAi or siRNA) has greater than 70% homology to CD40L, CD40R or  $\beta$ -amyloid.

30. The method of claim 28, wherein the interfering RNA (dsRNA, RNAi or siRNA) has greater than 95% homology to CD40L, CD40R or  $\beta$ -amyloid.

31. The method of claim 27, wherein gene fragments of CD40L, CD40R or  $\beta$ -amyloid are targeted with the interfering RNA (dsRNA, RNAi or siRNA), and wherein the gene fragments are approximately 15-25 nucleotides in length.

32. The method of claim 27, wherein gene fragments of CD40L, CD40R or  $\beta$ -amyloid are targeted with the interfering RNA (dsRNA, RNAi or siRNA), and wherein the gene fragments are greater than 25 nucleotides in length.
33. The method of claim 27, wherein gene fragments of CD40L, CD40R or  $\beta$ -amyloid are targeted with the interfering RNA (dsRNA, RNAi or siRNA), and wherein the gene fragments are greater than 50 nucleotides in length.
34. The method of claim 27, wherein gene fragments of CD40L, CD40R or  $\beta$ -amyloid are targeted with the interfering RNA (dsRNA, RNAi or siRNA), and wherein the gene fragments are one nucleotide less than the full length gene of CD40L, CD40R or  $\beta$ -amyloid.
35. The method of claim 21, wherein the animal or human is afflicted with a disease or disorder selected from the group consisting of neuronal inflammation, brain injury, brain trauma, tauopathy, and an amyloidogenic disease.
36. The method of claim 35, wherein the amyloidogenic disease is selected from the group consisting of Alzheimer's disease, scrapie, transmissible spongiform encephalopathy, hereditary cerebral hemorrhage with amyloidosis Icelandic-type, hereditary cerebral hemorrhage with amyloidosis Dutch-type, familial Mediterranean fever, familial amyloid nephropathy with urticaria and deafness (Muckle-Wells syndrome), myeloma or macroglobulinemia-associated idiopathy associated with amyloid, familial amyloid polyneuropathy (Portuguese), familial amyloid cardiomyopathy (Danish), systemic senile amyloidosis, familial amyloid polyneuropathy (Iowa), familial amyloidosis (Finnish), Gerstmann-Strausner-Scheinker syndrome, medullary carcinoma of thyroid, isolated atrial amyloid, Islets of Langerhans, diabetes Type II, and insulinoma.
37. The method of claim 35, wherein the tauopathy is selected from the group consisting of Alzheimer's disease, frontotemporal dementia, frontotemporal dementia with Parkinsonism, frontotemporal lobe dementia, pallidopontonigral degeneration, progressive supranuclear palsy, multiple system tauopathy, multiple system tauopathy with presenile dementia, Wilhelmsen-Lynch disease, disinhibition-dementia-parkinsonism-amyotrophy complex, Pick's disease, and Pick's disease-like dementia.

38. The method of claim 21, wherein the animal is a non-transgenic animal or a transgenic animal selected from the group consisting of worms, flies or mice.

39. The method of claim 38, wherein the transgenic animal expresses transgenic APP, overexpresses transgenic presenilin protein, overexpresses CD40R, overexpresses transgenic CD40L, and/or expresses tau protein or mutants thereof.

40. A method of identifying compounds and/or small molecules that reduce, ameliorate, or modulate signs and/or symptoms associated with neuronal inflammation, brain injury, brain trauma, tauopathies, or amyloidogenic diseases, comprising administering a compound that modulates the CD40L/CD40R signaling pathway to an animal, human or system and measuring or observing the reduction, amelioration, or modulation of the symptoms.

41. The method of claim 40, wherein the compounds and/or small molecules are compounds and/or small molecules that bind to CD40R, compounds and/or small molecules that bind to CD40L, compounds and/or small molecules that decrease trimerization of CD40R, compounds and/or small molecules that decrease trimerization of CD40L, compounds and/or small molecules that modulate the CD40L/CD40R signaling pathway upstream or downstream of CD40L/CD40R interaction, compounds and/or small molecules that reduce the phosphorylation of the tau protein or mutants thereof, compounds and/or small molecules that interfere with TNF receptor-associated factors, compounds and/or small molecules that interfere with presenilin-1 and/or presenilin-2, compounds and/or small molecules that inhibit  $\beta$ -secretase activity, compounds and/or small molecules that inhibit  $\gamma$ -secretase activity, compounds and/or small molecules that enhance  $\alpha$ -secretase activity, compounds and/or small molecules that alter APP processing, compounds and/or small molecules that reduce the ratio of APP  $\beta$ -CTF to APP  $\alpha$ -CTF, compounds and/or small molecules that reduce the amount of  $\beta$ -CTF, compounds and/or small molecules that promote brain-to-blood clearance of  $\beta$ -amyloid, compounds and/or small molecules that increase circulating levels of  $\beta$ -amyloid, compounds and/or small molecules that reduce the size and/or number of amyloid plaques, compounds and/or small molecules that reduce  $\beta$ -amyloid burden, compounds and/or small molecules that reduce soluble  $\beta$ -amyloid levels, compounds and/or small molecules that reduce total  $\beta$ -amyloid levels, compounds and/or small molecules

that reduce congophilic  $\beta$ -amyloid deposits, compounds and/or small molecules that reduce reactive gliosis, microgliosis, astrogliosis, and combinations thereof, a soluble CD40R compound, a soluble CD40L compound, an immunogenic CD40L compound, a soluble CD40LV compound, an interfering RNA (dsRNA, RNAi or siRNA) compound to CD40R, an antisense RNA compound to CD40R, an interfering RNA (dsRNA, RNAi or siRNA) compound to CD40L, an antisense RNA compound to CD40L or combinations of interfering RNA (dsRNA, RNAi or siRNA) compounds and antisense compounds, or a compound selected from the group consisting of agonistic antibodies to CD40R, agonistic antibodies to CD40L, antagonistic antibodies to CD40R and antagonistic antibodies to CD40L.

42. The method of claim 41, wherein the interfering RNA (dsRNA, RNAi or siRNA) comprises polynucleotide sequences identical or homologous to CD40L, CD40R or  $\beta$ -amyloid.

43. The method of claim 42, wherein the interfering RNA (dsRNA, RNAi or siRNA) has greater than 70% homology to CD40L, CD40R or  $\beta$ -amyloid.

44. The method of claim 42, wherein the interfering RNA (dsRNA, RNAi or siRNA) has greater than 95% homology to CD40L, CD40R or  $\beta$ -amyloid.

45. The method of claim 41, wherein gene fragments of CD40L, CD40R or  $\beta$ -amyloid are targeted with the interfering RNA (dsRNA, RNAi or siRNA), and wherein the gene fragments are approximately 15-25 nucleotides in length.

46. The method of claim 41, wherein gene fragments of CD40L, CD40R or  $\beta$ -amyloid are targeted with the interfering RNA (dsRNA, RNAi or siRNA), and wherein the gene fragments are greater than 25 nucleotides in length.

47. The method of claim 41, wherein gene fragments of CD40L, CD40R or  $\beta$ -amyloid are targeted with the interfering RNA (dsRNA, RNAi or siRNA), and wherein the gene fragments are greater than 50 nucleotides in length.

48. The method of claim 41, wherein gene fragments of CD40L, CD40R or  $\beta$ -amyloid are targeted with the interfering RNA (dsRNA, RNAi or siRNA), and wherein the gene fragments are one nucleotide less than the full length gene of CD40L, CD40R or  $\beta$ -amyloid.

49. The method of claim 48, wherein the signs and/or symptoms are a decrease in neuronal inflammation, a decrease in the trimerization of CD40R, a decrease in the trimerization of CD40L, modulation of the CD40L/CD40R signaling pathway upstream or downstream of CD40L/CD40R interaction, a reduction in the phosphorylation of the tau protein or mutants thereof, interference with TNF receptor-associated factors, interference with presenilin-1 and/or presenilin-2, that inhibition of  $\beta$ -secretase activity, inhibition of  $\gamma$ -secretase activity, enhancement of  $\alpha$ -secretase activity, alteration of APP processing, reduction in the ratio of APP  $\beta$ -CTF to APP  $\alpha$ -CTF, reduction in the amount of  $\beta$ -CTF, promotion of brain-to-blood clearance of  $\beta$ -amyloid, an increase in circulating levels of  $\beta$ -amyloid, or signs and/or symptoms selected from the group consisting of a reduction in the size and/or number of amyloid plaques, a reduction in  $\beta$ -amyloid burden, a reduction in soluble  $\beta$ -amyloid levels, a reduction in total  $\beta$ -amyloid levels, a reduction in congophilic  $\beta$ -amyloid deposits, a reduction in reactive gliosis, microgliosis, astrogliosis, and combinations thereof.

50. The method of claim 48, wherein the amyloidogenic disease is selected from the group consisting of Alzheimer's disease, scrapie, transmissible spongiform encephalopathy, hereditary cerebral hemorrhage with amyloidosis Icelandic-type, hereditary cerebral hemorrhage with amyloidosis Dutch-type, familial Mediterranean fever, familial amyloid nephropathy with urticaria and deafness (Muckle-Wells syndrome), myeloma or macroglobulinemia-associated idiopathy associated with amyloid, familial amyloid polyneuropathy (Portuguese), familial amyloid cardiomyopathy (Danish), systemic senile amyloidosis, familial amyloid polyneuropathy (Iowa), familial amyloidosis (Finnish), Gerstmann-Sträussler-Scheinker syndrome, medullary carcinoma of thyroid, isolated atrial amyloid, Islets of Langerhans, diabetes Type II, and insulinoma.

51. The method of claim 48, wherein the tauopathy is selected from the group consisting of Alzheimer's disease, frontotemporal dementia, frontotemporal dementia with Parkinsonism, frontotemporal lobe dementia, pallidopontonigral degeneration, progressive

supranuclear palsy, multiple system tauopathy, multiple system tauopathy with presenile dementia, Wilhelmsen-Lynch disease, disinhibition-dementia-parkinsonism-amyotrophy complex, Pick's disease, and Pick's disease-like dementia.

52. The method of claim 48, wherein the animal is a non-transgenic animal or a transgenic animal selected from the group consisting of worms, flies or mice.

53. The method of claim 52, wherein the transgenic animal expresses transgenic APP, overexpresses transgenic presenilin protein, overexpresses CD40R, overexpresses transgenic CD40L, and/or expresses tau protein or mutants thereof.

54. A method of treating neuronal inflammation, brain injury, brain trauma, tauopathies, amyloidogenic diseases, or internal organ diseases related to amyloid plaque formation, in an individual, comprising administering to an individual therapeutically effective amounts of a composition comprising a carrier and an agent that interferes with the CD40L/CD40R signaling pathway or the phosphorylation of tau protein.

55. The method of claim 54, wherein the agent is a compound that binds to CD40R, a compound that binds to CD40L, a compound that decreases trimerization of CD40R, a compound that decreases trimerization of CD40L, a compound that modulates the CD40L/CD40R signaling pathway upstream or downstream of CD40L/CD40R interaction, a compound that reduces the phosphorylation of the tau protein or mutants thereof, a compound that interferes with TNF receptor-associated factors, a compound that interferes with presenilin-1 and/or presenilin-2, a compound that inhibits  $\beta$ -secretase activity, a compound that inhibits  $\gamma$ -secretase activity, a compound that enhances  $\alpha$ -secretase activity, a compound that alters APP processing, a compound that reduces the ratio of APP  $\beta$ -CTF to APP  $\alpha$ -CTF, a compound that reduces the amount of  $\beta$ -CTF, a compound that promotes brain-to-blood clearance of  $\beta$ -amyloid, a compound that increases circulating levels of  $\beta$ -amyloid, a compound that reduces the size and/or number of amyloid plaques, a compound that reduces  $\beta$ -amyloid burden, a compound that reduces soluble  $\beta$ -amyloid levels, a compound that reduces total  $\beta$ -amyloid levels, a compound that reduces congophilic  $\beta$ -amyloid deposits, a compound that reduces reactive gliosis, microgliosis, astrogliosis, and combinations thereof, and a compound selected from the group consisting of CD40L, soluble CD40R, soluble

CD40L, immunogenic CD40L, CD40L variants (CD40LV), an antibody that binds to CD40L and blocks its interaction with CD40R, an antibody that binds with CD40R and blocks ligand binding to CD40R, a soluble CD40LV compound that binds to CD40R and fails to activate CD40R, an interfering RNA (dsRNA, RNAi or siRNA) compound to CD40R, an antisense RNA compound to CD40R, an interfering RNA (dsRNA, RNAi or siRNA) compound to CD40L, an antisense RNA compound to CD40L, or combinations of interfering RNA (dsRNA, RNAi or siRNA) compounds and antisense compounds.

56. The method of claim 55, wherein the interfering RNA (dsRNA, RNAi or siRNA) comprises polynucleotide sequences identical or homologous to CD40L, CD40R or  $\beta$ -amyloid.

57. The method of claim 56, wherein the interfering RNA (dsRNA, RNAi or siRNA) has greater than 70% homology to CD40L, CD40R or  $\beta$ -amyloid.

58. The method of claim 56, wherein the interfering RNA (dsRNA, RNAi or siRNA) has greater than 95% homology to CD40L, CD40R or  $\beta$ -amyloid.

59. The method of claim 55, wherein gene fragments of CD40L, CD40R or  $\beta$ -amyloid are targeted with the interfering RNA (dsRNA, RNAi or siRNA), and wherein the gene fragments are approximately 15-25 nucleotides in length.

60. The method of claim 55, wherein gene fragments of CD40L, CD40R or  $\beta$ -amyloid are targeted with the interfering RNA (dsRNA, RNAi or siRNA), and wherein the gene fragments are greater than 25 nucleotides in length.

61. The method of claim 55, wherein gene fragments of CD40L, CD40R or  $\beta$ -amyloid are targeted with the interfering RNA (dsRNA, RNAi or siRNA), and wherein the gene fragments are greater than 50 nucleotides in length.

62. The method of claim 55, wherein gene fragments of CD40L, CD40R or  $\beta$ -amyloid are targeted with the interfering RNA (dsRNA, RNAi or siRNA), and wherein the gene fragments are one nucleotide less than the full length gene of CD40L, CD40R or  $\beta$ -amyloid.

63. The method of claim 62, wherein the amyloidogenic disease is selected from the group consisting of Alzheimer's disease, scrapie, transmissible spongiform encephalopathy, hereditary cerebral hemorrhage with amyloidosis Icelandic-type, hereditary cerebral hemorrhage with amyloidosis Dutch-type, familial Mediterranean fever, familial amyloid nephropathy with urticaria and deafness (Muckle-Wells syndrome), myeloma or macroglobulinemia-associated idiopathy associated with amyloid, familial amyloid polyneuropathy (Portuguese), familial amyloid cardiomyopathy (Danish), systemic senile amyloidosis, familial amyloid polyneuropathy (Iowa), familial amyloidosis (Finnish), Gerstmann-Strausner-Scheinker syndrome, medullary carcinoma of thyroid, isolated atrial amyloid, Islets of Langerhans, diabetes Type II, and insulinoma.

64. The method of claim 62, wherein the tauopathy is selected from the group consisting of Alzheimer's disease, frontotemporal dementia, frontotemporal dementia with Parkinsonism, frontotemporal lobe dementia, pallidopontonigral degeneration, progressive supranuclear palsy, multiple system tauopathy, multiple system tauopathy with presenile dementia, Wilhelmsen-Lynch disease, disinhibition-dementia-parkinsonism-amyotrophy complex, Pick's disease, and Pick's disease-like dementia.

65. The method of claim 62, wherein the carrier is a pharmaceutically acceptable carrier or diluent.

66. The method of claim 62, wherein the route of administration of the composition to the individual is via parenteral, oral or intraperitoneal administration.

67. The method of claim 66, wherein the parenteral route of administration is selected from the group consisting of intravenous; intramuscular; interstitial; intra-arterial; subcutaneous; intraocular; intracranial; intraventricular; intrasynovial; transepithelial, including transdermal, pulmonary via inhalation, ophthalmic, sublingual and buccal; topical, including ophthalmic, dermal, ocular, rectal, and nasal inhalation via insufflation or nebulization.

68. The method of claim 66, wherein the composition of the carrier and the agent is administered orally in the form of hard or soft shell gelatin capsules, tablets, troches, sachets, lozenges, elixirs, suspensions, syrups, wafers, powders, granules, solutions or emulsions.

69. The method of claim 66, wherein the nasal administration of the composition of the carrier and the agent is selected from the group consisting of aerosols, atomizers and nebulizers.

70. The method of claim 66, further comprising administering the therapeutically effective amount of the composition of the agent and a carrier with other therapeutically effective compositions simultaneously or in intervals.

71. A method of causing a desired biological effect in an animal, human or system afflicted with neuronal inflammation, brain injury, brain trauma, a tauopathy, or an amyloidogenic disease, comprising the administration of a composition comprising a carrier and an agent that interferes with the CD40L/CD40R signaling pathway of the individual or system in amounts sufficient to cause the desired biological effect.

72. The method of claim 71, wherein the desired biological effect is a decrease in neuronal inflammation, a decrease in the trimerization of CD40R, a decrease in the trimerization of CD40L, modulation of the CD40L/CD40R signaling pathway upstream or downstream of CD40L/CD40R interaction, reduction in the phosphorylation of the tau protein or mutants thereof, interference with TNF receptor-associated factors, interference with presenilin-1 and/or presenilin-2, inhibition of  $\beta$ -secretase activity, inhibition of  $\gamma$ -secretase activity, enhancement of  $\alpha$ -secretase activity, alteration of APP processing, reduction in the ratio of APP  $\beta$ -CTF to APP  $\alpha$ -CTF, reduction in the amount of  $\beta$ -CTF, promotion of brain-to-blood clearance of  $\beta$ -amyloid, an increase in the circulating levels of  $\beta$ -amyloid, a decrease in  $\beta$ -amyloid levels in the central nervous system, reduction in the size and/or number of amyloid plaques, reduction of  $\beta$ -amyloid burden, reduction of soluble  $\beta$ -amyloid levels, reduction of total  $\beta$ -amyloid levels, reduction of congophilic  $\beta$ -amyloid deposits, reduction of reactive gliosis, reduction in microgliosis, reduction in astrogliosis, or any combination of the above-described biological effects.

73. The method of claim 71, wherein the amyloidogenic disease is selected from the group consisting of Alzheimer's disease, scrapie, transmissible spongiform encephalopathy, hereditary cerebral hemorrhage with amyloidosis Icelandic-type, hereditary cerebral hemorrhage with amyloidosis Dutch-type, familial Mediterranean fever, familial amyloid nephropathy with urticaria and deafness (Muckle-Wells syndrome), myeloma or macroglobulinemia-associated idiopathy associated with amyloid, familial amyloid polyneuropathy (Portuguese), familial amyloid cardiomyopathy (Danish), systemic senile amyloidosis, familial amyloid polyneuropathy (Iowa), familial amyloidosis (Finnish), Gerstmann-Strausner-Scheinker syndrome, medullary carcinoma of thyroid, isolated atrial amyloid, Islets of Langerhans, diabetes Type II, and insulinoma.

74. The method of claim 71, wherein the tauopathy is selected from the group consisting of Alzheimer's disease, frontotemporal dementia, frontotemporal dementia with Parkinsonism, frontotemporal lobe dementia, pallidopontonigral degeneration, progressive supranuclear palsy, multiple system tauopathy, multiple system tauopathy with presenile dementia, Wilhelmsen-Lynch disease, disinhibition-dementia-parkinsonism-amyotrophy complex, Pick's disease, and Pick's disease-like dementia.

75. The method of claim 71, wherein the agent is a compound that binds to CD40R, a compound that binds to CD40L, a compound that decreases trimerization of CD40R, a compound that decreases trimerization of CD40L, a compound that modulates the CD40L/CD40R signaling pathway upstream or downstream of CD40L/CD40R interaction, a compound that reduces the phosphorylation of the tau protein or mutants thereof, a compound that interferes with TNF receptor-associated factors, a compound that interferes with presenilin-1 and/or presenilin-2, a compound that inhibits  $\beta$ -secretase activity, a compound that inhibits  $\gamma$ -secretase activity, a compound that enhances  $\alpha$ -secretase activity, a compound that alters APP processing, a compound that reduces the ratio of APP  $\beta$ -CTF to APP  $\alpha$ -CTF, a compound that reduces the amount of  $\beta$ -CTF, a compound that promotes brain-to-blood clearance of  $\beta$ -amyloid, a compound that increases circulating levels of  $\beta$ -amyloid, a compound that reduces the size and/or number of amyloid plaques, a compound that reduces  $\beta$ -amyloid burden, a compound that reduces soluble  $\beta$ -amyloid levels, a compound that reduces total  $\beta$ -amyloid levels, a compound that reduces congophilic  $\beta$ -amyloid deposits, a

compound that reduces reactive gliosis, microgliosis, astrogliosis, and combinations thereof, and a compound selected from the group consisting of CD40R, CD40L, soluble CD40L, immunogenic CD40L, CD40L variants (CD40LV), antibodies that bind to CD40L and block its interaction with CD40R, antibodies that bind with CD40R and block ligand binding to CD40R, soluble CD40LV that bind to CD40R and fail to activate CD40R, interfering RNA (dsRNA, RNAi or siRNA) to CD40R, antisense RNA to CD40R, interfering RNA (dsRNA, RNAi or siRNA) to CD40L, antisense RNA to CD40L, and combinations thereof.

76. The method of claim 75, wherein the interfering RNA (dsRNA, RNAi or siRNA) comprises polynucleotide sequences identical or homologous to CD40L, CD40R or  $\beta$ -amyloid.

77. The method of claim 76, wherein the interfering RNA (dsRNA, RNAi or siRNA) has greater than 70% homology to CD40L, CD40R or  $\beta$ -amyloid.

78. The method of claim 76, wherein the interfering RNA (dsRNA, RNAi or siRNA) has greater than 95% homology to CD40L, CD40R or  $\beta$ -amyloid.

79. The method of claim 75, wherein gene fragments of CD40L, CD40R or  $\beta$ -amyloid are targeted with the interfering RNA (dsRNA, RNAi or siRNA), and wherein the gene fragments are approximately 15-25 nucleotides in length.

80. The method of claim 75, wherein gene fragments of CD40L, CD40R or  $\beta$ -amyloid are targeted with the interfering RNA (dsRNA, RNAi or siRNA), and wherein the gene fragments are greater than 25 nucleotides in length.

81. The method of claim 75, wherein gene fragments of CD40L, CD40R or  $\beta$ -amyloid are targeted with the interfering RNA (dsRNA, RNAi or siRNA), and wherein the gene fragments are greater than 50 nucleotides in length.

82. The method of claim 75, wherein gene fragments of CD40L, CD40R or  $\beta$ -amyloid are targeted with the interfering RNA (dsRNA, RNAi or siRNA), and wherein the gene fragments are one nucleotide less than the full length gene of CD40L, CD40R or  $\beta$ -amyloid.

83. The method of claim 71, wherein the agent is an anti-CD40R antibody.
84. The method of claim 80, wherein the anti-CD40R antibody is one or more species of monoclonal anti-CD40R antibodies, polyclonal antibodies to CD40R, or a combination of polyclonal and monoclonal antibodies.
85. The method of claim 71, wherein the agent is an anti-CD40L antibody.
86. The method of claim 85, wherein the anti-CD40L antibody is one or more species of monoclonal anti-CD40L antibodies, polyclonal antibodies to CD40L, or a combination of polyclonal and monoclonal antibodies.
87. The method of claim 71, wherein the carrier is a pharmaceutically acceptable carrier or diluent.
88. The method of claim 71, wherein the route of administration of the composition to the individual is via parenteral, oral or intraperitoneal administration.
89. The method of claim 88, wherein the parenteral route of administration is selected from the group consisting of intravenous; intramuscular; interstitial; intra-arterial; subcutaneous; intraocular; intracranial; intraventricular; intrasynovial; transepithelial, including transdermal, pulmonary via inhalation, ophthalmic, sublingual and buccal; topical, including ophthalmic, dermal, ocular, rectal, and nasal inhalation via insufflation or nebulization.
90. The method of claim 88, wherein the composition of the carrier and the agent is administered orally in the form of hard or soft shell gelatin capsules, tablets, troches, sachets, lozenges, elixirs, suspensions, syrups, wafers, powders, granules, solutions or emulsions.
91. The method of claim 89, wherein the nasal administration of the composition of the carrier and the agent is selected from the group consisting of aerosols, atomizers and nebulizers.

92. The method of claim 71, further comprising administering the therapeutically effective amount of the composition of the agent and a carrier with other therapeutically effective compositions simultaneously or in intervals.